

## IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicants : Simons *et al.*  
Serial No. : 09/145,916  
Filed : September 2, 1998  
For : "STIMULATION OF ANGIOGENESIS VIA  
ENHANCED ENDOTHELIAL EXPRESSION  
OF SYNDECAN-4 PROTEINS"  
Examiner : David Guzo  
Group Art Unit : 1636  
Attorney's Docket No : BIS-039

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on: Feb. 6, 2002

Attorney for applicants:

David Traskler

Signature:

David Traskler

Date:

Feb. 6, 2002

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MARKED UP VERSION OF AMENDED SPECIFICATION SUBMITTED  
PURSUANT TO 37 C.F.R. 1.121(b)

Assistant Commissioner for Patents  
Washington, D.C. 20231

Sir:

Applicants, in fulfillment of and in accordance with the requirements  
of 37 C.F.R. 121(b)(iii), hereby submit a marked up version of the instant

amendment to the Specification via marked-up replacement paragraphs,  
this Specification amendment being directed to the paragraph at:

Page 29, line 23.

Respectfully submitted,

SIMONS *et al.*

By: 

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1 C. The Cytoplasmic Domain Coding For The Syndecan-4 Peptide

2  
3 The third requisite cytoplasmic domain must code for the amino acid  
4 residue structure representative of the syndecan-4 core protein. As shown  
5 experimentally by the data presented hereinafter, only the syndecan-4 cytoplasmic  
6 region and peptide structure allows for functional stimulation of angiogenesis in-  
7 situ. For this reason, it is essential and required in each embodiment of the  
8 present invention that the third DNA sequence coding for the cytoplasmic domain  
9 in the expressed proteoglycan entity in a transfected endothelial cell be  
10 representative of and analytically identifiable as the syndecan-4 amino acid residue  
11 structure. A representative recitation of the DNA constituting the cytoplasmic  
12 domain of the syndecan-4 molecule is presented by Fig. 13 herein.

13 It will be noted and recognized that very little variability and substitution  
14 within the specific DNA base sequencing of the cytoplasmic domain of the  
15 syndecan-4 molecule is permitted. While some changes are expected, be they  
16 point mutations, block substitutions and the like, the expected or envisioned degree  
17 of variability which might be present or permitted for the cytoplasmic domain  
18 DNA is believed to be quite limited.

19 As representative examples: The last four amino acids (EFYA) cannot be  
20 changed or modified. Similarly, regarding the Serine residue at position 181: a  
21 mutation to an Alanine residue potentiates activation; while a mutation to  
22 Glutamate inhibits cell growth in a dominant fashion (dominant-negative mutation).  
23 Finally, the LGKKPIYKK sequences [SEQ ID NO:24] probably cannot be altered at  
24  
25 all.